for eight hours have been studied clinically. Thirty-seven of these cases have been the subject of a detailed clinical, haematological and biochemical investigation.

(2) The most constant and prominent features have been the development of anoxia and bilirubinaemia, progressing to manifest clinical jaundice in thirty-seven cases. Hippuric acid tests show a considerable reduction in liver function.

(3) Continuous oxygen and carbon dioxide therapy lessens but does not abolish the features of anoxia. The administration of oxygen and carbon dioxide does appear however to prevent the development of circulatory collapse. The prevention of liver damage is discussed. Vomiting has become less frequent since oxygen therapy was introduced.

(4) This complication of circulatory collapse is a failure of the vasomotor and respiratory centres and is not due to a reduction in the circulating blood volume or to myocardial failure. Morphine is absolutely contra-indicated.

(5) There is a transient polymorphonuclear leucocytosis and a transient haemodilution.

(6) There is a small transient rise in non-protein nitrogen and a tendency for plasma chlorides and urinary chlorides to fall.

(7) Indications for terminating treatment and recommendations for pre-hypertherm and post-hypertherm treatment are formulated.

(8) Sulphathiazole premedication with 6 grammes of the drug does not increase the hazards of this treatment.

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DISCUSSION ON THE PRECEDING PAPERS

Lt.-col. **C. M. Spooner**, R.A.M.C., said that pyretotherapy had been commenced at No. 1 Canadian General Hospital about fifteen months previously. All the patients treated suffered from persistent and chemo-resistant urethritis with gonococci present in the secretion. In addition a number of cases of gonorrhoeal arthritis and of gonorrhoeal proctitis had been treated. Three hundred and six fever sessions had been given to 176 patients. He had looked up the records of 100 consecutive cases of gonorrhoeal urethritis to compare with Lt.-col. King's figures. In sixty-five of the 100 cases a satisfactory eight-hour fever session was accomplished. In thirty-five cases the fever session was not completed. Of the sixty-five patients receiving an adequate fever session fifty-seven were completely cured; in six cases a second session was required and there were two cases classified as complete failures. The number of days in hospital prior to hyperthermy averaged forty-nine; the pre-pyrexial chemotherapy with a sulphonamide averaged 82·5 grammes; one patient had received a total of 333·5 grammes of sulphonamide previous to pyrexial treatment. In thirty-five cases they were unable to give a satisfactory session of fever

and in fifteen of these this failure was due to lack of cooperation on the part of the patient. If the cases had been more carefully selected there is no doubt that there would have been fewer failures. In five cases failure was due to mechanical breakdown of the apparatus. In fifteen cases treatment was discontinued because of physical deterioration of the patient. In eight of these cases there was some disturbance of the cardiovascular system ; in three, symptoms of nervous origin ; in two, heat cramps, and in two cases, persistent uncontrolled vomiting. Out of these thirty-five patients inadequately treated by fever therapy sixteen were completely cured and twelve were considered to be markedly improved. The patients were discharged from hospital within sixteen days without symptoms or signs. There was complete failure in seven cases. There were satisfactory results in 91 per cent of the cases ; however on examining subsequent records he found that two of the six cases were re-admissions to hospital with gonorrhoea. Lt.-col. Spooner felt sure that six were re-infections although they were recorded as failures, thereby reducing the percentage of complete cures to eighty-nine which corresponded to Lt.-col. King's percentage of cure. His unit had experienced much the same complications and reactions as had Lt.-col. King's, but with one notable exception : jaundice had been a very uncommon complication. The serum bilirubin was estimated in 124 cases and only in one case was there noted an elevation above the high normal ; in another case a slight elevation to high normal reading after hyperthermy was recorded. The first patient had an initial rise before the onset of pyrexia and a marked rise afterwards, accompanied by clinical jaundice which rapidly disappeared. He felt that the administration of concentrated glucose solution intravenously was of use in decreasing the restlessness of the patient and benefiting his general condition. The preliminary preparation of the patient was important. All patients were given a high calorific diet which was reinforced by vitamins A and B_1. The administration of this last vitamin may account for the low incidence of jaundice. There had not been any deaths but there had been three serious reactions. One was due to heatstroke which resulted in the patient being completely comatose for thirty-six hours but subsequently he made a complete recovery. The other two reactions were of cardiovascular nature and responded to appropriate measures.

The President, Brig. **T. E. Osmond**, said members had heard enough about hyperthermy to convince them that it was an almost essential weapon in their armamentarium against venereal disease, especially in the case of patients who resisted sulphonamide treatment ; he hoped that members would be stimulated to use it.

Dr. **G. M. Thomson** said that in Edinburgh they had used an Inductotherm cabinet for the production of artificial pyrexia in seventy-one resistant cases. Fifty-four patients completed this treatment which was a little different from that already outlined. The patients had a thorough investigation including an X-ray examination of the chest which was essential before submitting patients to fever therapy. The infected focus must also be identified because it made a great difference to the prognosis whether there was a prostatitis or an infiltration into the urethra or no recognizable complicating factor, in other words, whether or not a true drug-resistant case was under consideration.

The majority of the patients came from a military hospital and had been previously treated for an average period of eight weeks, the maximum being eighteen, and the minimum two. Several patients from an allied naval hospital were included, but on account of the language difficulties treatment was discontinued in a larger proportion than in the case of the British patients. The reasons for stopping the treatment were blistering of the skin, six cases ; vomiting, two cases ; non-cooperation, five cases ; tachycardia, two cases ; cyanosis, one case ; and tetany, one case ; total seventeen cases. Blistering of the skin was mostly due to a war-time shortage of trained nursing staff. On the day before the patient went into the fever cabinet he was given from 6 to 8 grammes of sulphapyridine intravenously, the amount depending upon his weight. At 11 p.m. he was given 4 tablets of sulphapyridine, at 6 a.m. next morning another 4 tablets by mouth and during the session another 6 grammes of soluble sulphapyridine intravenously. After the treatment was finished additional tablets were given, provided they could be tolerated, up to a total of 25 grammes. This total was considerably more than that used by other workers. The blood concentration of the sulphonamide had been measured and was between 5 and 10 milligrams per cent at the height of the fever.

He had not found it necessary to use oxygen, but it might have been of value in certain of the cases in which the treatment was stopped. The temperature rose more slowly, taking two hours to reach 106°F., and he thought the slower rise was beneficial because it distressed the patient less and was less likely to produce tachycardia. Glucose was given, 6 per cent, in 0·9 per cent saline by mouth. Ice packs and iced drinks were frequently used and were well tolerated. Dr. Thomson was surprised to hear that morphine should not be used as he had found it effective and without appreciable ill effects. In this series jaundice had not been noted. There had been one case of facial palsy. He wondered whether the symptoms of anoxia might be produced by some action in the skin because of the higher rate of temperature elevation used in the Kettering Hypertherm. In the Inductotherm the temperature was taken up by a very short wave and high frequency current of 12 million cycles per second. The anoxia might be due to some histo-toxic products, liberated from the skin by the higher air temperature in the Kettering Hypertherm and which would account to some extent for the vomiting.

Coming to results, of the fifty-four patients who tolerated treatment of eight hours, three relapsed later and showed gonococci present in the smears. The observation period extended for seven and a half days in hospital and was followed by the routine three months' survey. The final cure rate was 94 per cent, which was a little higher than those mentioned. This might, however, be due to the small series of cases so far dealt with.

Dr. **A. H. Harkness** said that in the hands of an expert the death rate following fever induced by physical methods was not high, especially with the air-conditioned cabinet ; but many deaths were still being recorded in the literature, and today they had heard of two more. Pelouze stated that fatalities in the United States of America were not always reported in the literature and that he knew of fourteen unpublished deaths from this cause. Since gonorrhoea was not a fatal disease the large majority of the deaths recorded were directly due to treatment. For drug-resistant cases he stressed the importance of mild protein shock by the intramuscular injection of a vaccine or of Aolan during the chemotherapy trial period which lessened considerably the number requiring more drastic treatment. This method would occasionally effect a cure and it often mobilized the defence mechanism so that further chemotherapy was successful. When this treatment failed, general reactions with sharp rises in temperature were essential and to produce these he preferred the intravenous injection of a vaccine. It was not necessary to admit the patient to hospital and the dangers were considerably less than from fever induced by physical methods. Did the Hypertherm desensitize patients who had previously shown a sensitization to one or more sulphonamide drugs ? In his experience this did not follow fever induced by the intravenous injection of a vaccine. Lt.-col. King was in agreement with Simpson, Kendell and Rose concerning the advantages of the combination of fever and chemotherapy. This had not been the speaker's experience with fever induced by the intravenous injection of a vaccine. When the sulphonamides failed they undoubtedly interfered with the defence mechanism of the host, since local treatment, which, in the pre-sulphonamide period always controlled the infection, now appeared ineffective. Was it wise to continue with the drug while an effort was being made to stimulate the defence mechanism of the host ? He considered that better results followed when fever and chemotherapy were not prescribed together. Trautman obtained better results in the treatment of gonococcal arthritis with fever alone. Dr. Harkness considered that there must be few cases of non-specific urethritis requiring fever treatment. We had not been told of the nature of the organisms responsible for the urethritis. He was particularly interested in urinary infections due to *Streptococcus faecalis* which were always resistant to the sulphonamides. Did the hypertherm cure any of these conditions ? In his opinion no patient with non-specific urethritis should be given fever before a thorough investigation of the upper and lower urinary tract had been made, for some of these patients suffered from calculi or other serious lesions of the upper urinary tract.

Lt.-col. **King** said that no secret was made of the dangers in this treatment but he maintained that they could be eliminated by skill and experience. The deaths occurred at a stage at which technique had not reached its present level of efficiency. Dr. Harkness considered that such patients should be treated with protein shock and he could assure him that in most of the cases intravenous injections of T.A.B. vaccine had been tried before the mechanical fever was used. Dr. Harkness seemed to think that the use of the combination of sulphonamides and fever was unsound in theory, but the figures presented spoke for themselves. The results obtained with the combination of mechanical fever and a sulphonamide, as opposed to fever without a sulphonamide, had proved that point beyond question. As a general rule a sulphonamide was not used in combination with intravenous T.A.B. vaccine although this had been done for a short time for the purpose of investigation. The majority of patients treated were suffering from straightforward resistant urethritis. All cases in which there was any reason to suspect an upper urinary tract infection had been investigated from that standpoint, although such investigation was not a routine. Until recently first-class culture work had not been possible and in these cases of non-specific urethritis no record of the causative organism was available.

Maj. **D. I. Williams** said Capt. Wallace had stressed that the work he did was twelve months old. Experience had increased considerably since then and certain of his recommendations today were already in use. The treatment differed from that of twelve months ago ; they now treated at 106° F. and not 106·6° F. ; this reduction had made a decisive difference to the incidence of complications. The incidence of complications mentioned by Capt. Wallace was accurate for that time, but not for the whole series. The figures which he quoted for circulatory collapse of 17 per cent covered many cases occurring after treatment in which intravenous saline had been given. Reactions followed and it was thought that the accompanying rigor was responsible for the subsequent circulatory collapse. There had also been a reduction in the incidence of jaundice since the temperature was reduced to 106° F. Of the thirty-one patients quoted as having jaundice, all except two were treated at the 106·6° F. level, and of the thirty-nine at that level, all except two had considerable rises above 106·6° F. In the last six months they had had only three cases of clinical jaundice, and sub-clinical jaundice now occurred in just over half the number of patients treated. Capt. Wallace carried out hippuric acid tests in eight cases and found that every patient showed some defect of liver function. Tests were carried out in another forty cases on the day before treatment and again after treatment and in twenty-eight there was normal liver function after treatment as judged by this test.

Capt. **Wallace** referring to circulatory collapse said that he and Capt. Bushby were impressed that from the time of introduction of oxygen and carbon dioxide therapy circulatory collapse had not occurred. It was most important to use adequate oxygen therapy with the addition of carbon dioxide, especially for one to two hours after the termination of treatment. Maj. Williams had raised the question of reactions following the administration of intravenous fluids. Capt. Wallace stated that it was most important if any intravenous therapy was used that reliable pyrogen-free preparations must be obtained. It might be worth while giving some of these patients plasma infusions as a possible additional protection to the liver now that protein was regarded as an important factor in liver protection. He did not regard the danger of liver damage from plasma

itself as very great. Cases of hepatitis occasionally followed the administration of serum or plasma, but these cases were rare and there was a very long latent period between the administration of the protein fluid and the development of jaundice.

Maj. **Nicol** said he was interested to hear that in Lt.-col. Spooner's series there had been only one case of clinical jaundice and one case of sub-clinical jaundice. This disparity of experience they were, at the moment, unable to explain. With regard to Dr. Thomson's work in Edinburgh, in which he stressed the importance of X-ray examination of the chest before treatment, actually in a larger number of cases this examination had been done.

In some cases in the present series the concentration of sulphathiazole in the blood was estimated before and after treatment. It was found that a satisfactory blood concentration was obtained in the majority of cases by giving 6 grammes of sulphathiazole in the eighteen hours before fever. The attainment of similar concentrations had been reported by Simpson, Kendell and Rose, following slightly larger amounts of sulphathiazole as premedication. Maj. Nicol and his colleagues had not used morphine in these cases so that no opinion could be given on its effects. Dr. Thomson had also suggested that the incidence of jaundice might be due to the cabinet temperature of the Kettering Hypertherm being higher than that employed in the Inductotherm. Dr. Thomson did not quote the Inductotherm cabinet temperature but in the Hypertherm, with present modifications, the cabinet temperature was extremely low. Maj. Nicol thought that in cases like those described by Dr. Thomson, in which there was a certain number of skin burns, histo-toxic reactions would be more likely to occur than in the present series in which skin burns had been relatively uncommon. He had noted, when using T.A.B. vaccine to produce low fever reactions in cases of treated gonorrhoea in which the gonococcus was no longer present in the urethral smears, that gonococci had reappeared in some cases, while in others further sulphonamide therapy had produced clinical cure. He could not explain why low fever sometimes seemed to provoke the gonococcus whereas high and long fever seemed to make it disappear. Lt.-col. King had pointed out that many patients who were ultimately treated by hyperthermy had had T.A.B. vaccine administered previously. Capt. Wallace had discussed the giving of plasma to prevent jaundice. They agreed that protein and amino-acids, especially the sulphur-containing ones, should be given, as they might be expected to protect the liver but it was more satisfactory to give them by mouth in a diet with a high sulphur-containing amino-acid content than to give plasma which possessed certain dangers.

Capt. **Wallace** said that oral fluids were most suitable but if it was necessary to give fluids intravenously it was important to choose fluids which were properly prepared. He had noticed that there was not much danger in giving rapid intravenous infusions to such patients, provided they were observed carefully for any signs of developing cardiac failure. There had been no evidence of myocardial damage in such cases.

Dr. **Thomson** said that the temperature in the Inductotherm never exceeded 110° F., whereas in the Kettering Hypertherm he believed it was 120° F. or 130° F. The air saturation in the cabinet was about 85 per cent.

Wg.-cdr. **McElligott** suggested, with regard to the cause of facial palsy, that these were cases of ordinary Bell's palsy caused by the continual blowing of the electric fan on the patient's face throughout the eight hours' treatment.

Dr. **Thomson** stated that he had seen a case in which facial palsy occurred on the side of the face nearest to the fan.

Dr. **Shanson** asked whether sulphathiazole could become a more potent drug in a patient undergoing fever treatment.

Lt.-col. **A. G. Johnson** said that the Kettering Hypertherm was not available to many in wartime and the fact that some patients were cured as a result of fever produced by a simple hot bath was of interest. The President himself had directed the speaker's notice to a description of this method in an American paper. The technique contained therein was elaborate, as it required cultures of the resistant organism being subjected to experimental temperatures for a sufficient time to kill it and then subjecting the patient to similar conditions. He had obtained good results by using an ordinary hot bath, which raised the mouth temperature to 106° F., on two or three successive days, together with a course of a sulphonamide. Thirty-four patients had been treated in this way, with success in twenty-four. All the cases had previously been treated with two or more sulphonamides, including sulphathiazole. None had been treated with intravenous T.A.B. vaccine because he had abandoned that method. At a bath temperature of 110° F. the patient's temperature rose to 104° F. in about fifteen minutes ; the bath temperature was then increased to 112° F. and the patient's mouth temperature rose to 106° F. Depending upon his general condition, he was removed at that time or within a few minutes. This method might be of interest to those who had not access to a Kettering Hypertherm.

Dr. **Mascall** thought fever therapy was applicable only when one had ample staff, ample funds and ample bed accommodation. Civilian doctors in charge of an out-patient clinic, where staff were scarce and beds even scarcer, had to be satisfied with milder forms of treatment ; their results were not unsatisfactory. Brig. Osmond in a recent paper quoted 5 per cent of relapses with modern treatment. If he had to subject his clinic patients to fever treatment, the number of working hours lost per week would be colossal, and it was very important at the present time to keep people at their work. The admitting of a patient into hospital, which in this form of treatment was essential, often led to considerable domestic and family upsets. It was feasible in the Forces, when the patients were away from home, but in civilian practice it was a difficult matter, for often secrecy was necessary. He thought that the treatment was unnecessarily severe in an uncomplicated case of gonorrhoea for the patient was subjected to risks which the disease ordinarily

did not warrant. Even in drug-resistant cases a satisfactory result could be obtained with milder forms of induced pyrexia.

Dr. **Harkness**, in view of the remarks made by one speaker, reiterated that he still had to see a case in which chemotherapy failed after a course of T.A.B. vaccine injections. He considered that the time factor in these cases was very important and he did not think that fever should be induced before at least three weeks had elapsed.

THE NURSING ASPECT OF HYPERTHERMY TREATMENT

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Sister-in-Charge, Hyperthermy Department, at a Military Hospital

Patients selected for hyperthermy treatment are admitted to the special ward two days beforehand and are given a diet rich in protein, receiving the last meal at tea-time of the day before treatment. A cleansing enema is given the same evening. To those who are not sensitive to sulphonamide drugs, tablets of sulphathiazole or sulphadiazine are given in doses of two grammes at 4 p.m., 8 p.m., 12 midnight and 4 a.m., during the sixteen hours preceding treatment, the total dosage being therefore eight grammes.

Course of treatment

The working day in the Hyperthermy Department begins at approximately 7.20 a.m. The cabinets which have been preheated by the night staff are ready for use. The patient arrives at this time and while he undresses, the trolleys are prepared with the requirements of the day. Wearing a towel as a girdle, the patient is weighed; the rectal temperature, pulse, respirations and blood pressure are carefully taken and recorded. Dentures, rings and identity discs are removed and a careful scrutiny of the patient is made for any unfavourable signs, such as drug rashes, which might be a contra-indication to the proposed treatment. The cabinet, which should register a temperature of 120° F. to 124° F., is now opened and the patient is placed inside. His head, which projects through an aperture at one end of the cabinet, is made comfortable on one or more pillows; a towel is adjusted around the neck to prevent leakage of cabinet heat. The towel worn by the patient as a girdle lies loosely across the groins or may be removed altogether. The rectal thermometer which is connected to the Cambridge indicator is inserted into the anal canal.

Induction of fever.—The period of elevation of temperature which continues until the height of the fever (106° F.) is reached, usually takes from sixty to seventy minutes. A shorter induction period places a considerable strain on the patient's circulatory system and is therefore avoided. During induction the cabinet temperature should be limited to 116° F. and it is often necessary to dial down the cabinet switch control in order to obtain this level. From the beginning of the treatment the patient is encouraged to drink 200 cubic centimetres of 0·6 per cent solution of sodium chloride in water every fifteen minutes throughout the induction period. Afterwards a similar amount may be given every thirty minutes until a total of four litres of the fluid has been taken. If nausea occurs 0·3 per cent solution of sodium chloride is substituted, usually with good effect. An occasional drink of plain water may be given. To every patient without exception a mixture of oxygen, 93 per cent, and carbon dioxide, 7 per cent, is administered through a B.L.B. oro-nasal or nasal mask at the rate of nine litres each minute throughout the whole of the induction period.

The rectal temperature is carefully observed; the readings recorded on the indicator are frequently counterchecked by the additional insertion of a mercury thermometer. Temperature readings are charted at intervals of fifteen minutes during the periods of induction, maintenance and fall of the fever. Discomfort and slight restlessness are almost invariably experienced when the body temperature runs between 101° F. and 103° F. By this time the patient is perspiring pro-